sults of transfusion of blood in twenty-six patients with pernicious anemia who were followed over long periods of time. One hundred and one transfusions were given and individual patients received from one to seventeen, the largest total amount of blood being 8700 cc. and the smallest 300 cc. The single transfusions varied in amount from 300 to 900 cc. The results of this analysis brought out no evidence that the total duration of life was prolonged by the treatment, nor did transfusions seem to be of definite value as an emergency measure in tiding patients over at a time when the blood count was very low. Of nine patients entering the hospital with blood counts of under a million and receiving transfusion, six improved and left the hospital and three, or 33 1/3 per cent, died; whereas of ten other patients with counts under a million who did not receive transfusion, eight improved and two, or 20 per cent, died.

The most important conclusion seemed to be that the time when transfusion is done is of particular importance. If the patient is in a refractory state, which is usually the case during the relapse, transfusion seems to have little effect. On the other hand, if performed at a time when the patient was not refractory (i. e., when spontaneous remission was imminent or had commenced), improvement seemed to be brought on in about one-half the cases, and it was possible to raise the blood count to a higher level than it usually reaches spontaneously. Such artificial plethoras did not increase the duration of the remission, although the patients usually had a sense of well-being while the count was high.

As Falconer points out, the anemia is evidently only one of a number of harmful effects which are produced by whatever agent is responsible for pernicious anemia, and it is quite obvious that transfusions at best can do no more than aid in temporary improvement in selected cases.

ROY E. THOMAS, M. D. (1136 West Sixth Street, Los Angeles)—In the treatment of any disease it is difficult to see how the patient can be permanently benefited by a therapeutic measure directed against one of its symptoms.

Falconer has clearly shown in his paper that transfusion of blood does not materially prolong life in the great majority of cases of pernicious anemia in which it is used. He has gone a step further and given theoretical reasons for believing that no better results could be expected.

For obvious reasons it is particularly difficult to determine the value of any therapeutic measure in a disease which is characterized by spontaneous remissions. Only by such careful blood studies as Falconer has made can the reaction of the bone marrow to transfusions in pernicious anemia be determined and thus enable us to avoid their use when they are likely to prove of no benefit or even harmful.

I do not believe we are ready to dispense entirely with transfusions in pernicious anemia. Falconer states that they bring about 10 to 20 per cent more remissions than occur spontaneously. If this is true life is probably prolonged in some instances, for Lichty's view that every case of pernicious anemia has just so many remissions to look forward to seems absurd. Also many times transfusions seem to add much to the comfort of the patient and are thus quite worth while.

However, I have recently had the opportunity to observe for a considerable period three cases of pernicious anemia which had presented symptoms of the disease for 8, 12, and 15 years, respectively. One had a splenectomy followed by hydrochloric acid in large doses. The second had many transfusions which seemed to add much to her comfort. The third who has had neither splenectomy nor transfusions is the only one left alive to eat liver.

ERNEST S. DU BRAY, M. D. (University of California Medical School, San Francisco)—Falconer's timely warning about the thoughtless use of blood transfusion in the treatment of pernicious anemia is but a reflection of the opinion of many of the most careful students of the hematopoietic diseases. He has defined quite clearly the limitations of its use and at the same time he indicates certain pitfalls which may attend the method. It is pleasing to see that he stresses the point that the decision for or against transfusion is frequently a matter which demands extremely sound clinical judgment. Another important phase which he mentions and which I feel is worth re-emphasizing is the possibility of a severe reaction in a patient who, because of repeated transfusions, has developed antibodies for compatible bloods. It is now agreed that transfusion never cures pernicious anemia, and the patients in whom the best results are obtained are those who are most likely to have a spontaneous remission and who react best to any treatment. The procedure must be regarded as a useful and often effective method for the alleviation of distressing subjective symptoms, and in rare and carefully selected cases may even be a life-saving measure.

CHRONIC APPENDICITIS

A STUDY OF 202 CONSECUTIVE CASES

By HERSEL E. BUTKA *

"THERE are two types of appendicitis," says one author, "one acute, and the other for revenue only," while some others ask the question, "Is chronic appendicitis a myth?"

Investigators are at variance as to the pathological findings in chronic appendicitis. Ribberts states that the normal appendix is always empty, while Aschoff claims that 62 per cent of normal appendices contain feces. Roentgen ray examination shows that the appendix fills, empties, and alters its shape periodically. There may be pathological conditions present that cannot be proved by the anatomist or histologist, but can be demonstrated roentgenologically by the finding of a large open canal which fills easily but is unable to properly empty and retains this material over long periods of time.

The rôle of hard fecal material and foreign bodies in the pathogenesis of chronic appendicitis is somewhat disputed, but probably should be recognized. Because of the well-known frequency of these bodies in acute appendicitis, their presence will be considered proof of chronic appendicitis in this paper.

Eastman states that many cases of so-called chronic appendicitis must be considered as due to malposition, adhesions and kinks, with little microscopic pathology. Aschoff's description of changes in chronic appendicitis enumerates the findings briefly as "stenosis, induration of wall, retention of mucus, fecal masses, adhesions and kinking." He believes that chronic appendicitis is never primary but is always due to a previous acute attack or attacks, many times occurring during childhood and simply called "stomach ache."

According to Mallory, "during repair, the appendix is often infiltrated with numerous eosinophiles, and the lymph vessels filled with lymphocytes. The appearance presented by appendices in the various stages of repair is often spoken of as chronic appendicitis, but this term is not justified."

The microscopic appearance of the appendix varies normally. The coats vary in thickness with age. Lymphoid tissue is greatest in the young, while

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CHART No I

NATURE OF CASES

		Number	Sex		Temp.		Symptoms				Laboratory Findings					
											White Blood Count					
			M	F	Normal	Increased	Tenderness	Pain-Abd.	Rigidity	Vomiting	Number	Normal	Increased	Percent Polynuclear	Wassermann + +	Walkers. Index of Resist.
1 Appendicitis Chronic	No	81	30	51	29	52	68	51	47	21	12,667	40	41	79	2	−2.3
	%	40	37	63	36	64	84	63	58	26		49	51		2.4	
2 Cholecystitis	No	12	-	12	9	3	7	6	1	1	11.100	8	4	75	0	−1
	%	5.9	-	100	75	25	58	50	8.3	8.3		66	34		0	
3 Salpingitis	No	14		14	7	7	10	14	2	5	12.700	6	8	82	1	−1.5
	%	6.9		100	50	50	71.5	100	14	35		43	57		7	
4 Uterine Surgery	No	25		25	13	12	18	12	2	6	8.700	17	8	76	3	−3.5
	%	12.3		100	52	48	73	48	8	24		69	32		12	
5 Hernia	No	7	4	3	4	3	1	1	0	1	7,500	6	1	65	1	-
	%	3.4	57	43	57	43	14	14	0	14		86	14		14	
6 Miscellaneous	No	63	5	58	31	32	22	26	5	6	9250	42	21	75	3	−3.5
	%	31.2	8	92	49	51	34	41	8	9.5		66	33.3		5	

it atrophies in later years. Similar changes to a minor degree occur in the other coats.

With this brief introduction the following questions present themselves for our study:

(1) Is chronic appendicitis a clinical or pathological entity? (2) What changes are found in the atrophic and obliterated appendix? (3) Is the presence of eosinophiles in the apparently normal and so-called chronic appendicitis a pathological change? (4) Can chronic appendicitis be determined from a microscopic study of the organ?

This paper is a review of 202 consecutive surgical cases with appendectomy occurring in the White Memorial Hospital during a period of approximately two years. It was inspired by my study of many appendiceal sections that I might arrive at some conclusion as to the microscopic appearance of a normal appendix.

The cases are grouped as: (a) appendices removed from patients with clinical chronic appendicitis; (b) appendices in which operation was secondary to gall bladder disease; (c) appendices in which removal was secondary to inflammatory pelvic disease (salpingitis, etc.); (d) appendices removed during operation on uninflamed pelvic organs (uterus, etc.); (e) appendices removed during repair of hernia; and (f) miscellaneous.

Is chronic appendicitis a clinical or a pathological entity? In comparing the first group of the chart, which covers eighty-one patients diagnosed and operated on for chronic appendicitis without a change in diagnosis following operation, with the remaining series, I find a definite increase in average diameter of the appendix, as well as the number containing feces. There is apparently no variation in the number containing fecoliths. A few contain foreign bodies. A greater percentage show adhesions, kinks, Jackson's veil, or obliterative and atrophic changes. However, the differences between those appendices definitely normal as far as symptomatology is concerned, and those diagnosed as chronic appendicitis, are not marked. The finding of adhesions, kinks, Jackson's veil, hard feces, foreign bodies and mucus would account for only 34 per cent of those diagnosed as chronic appendicitis, while in Groups 4 and 6 there are 40 per cent and 41 per cent, respectively, revealing some of these changes.

In view of these findings I conclude that chronic appendicitis must be frequently functional, and is more of a clinical than a pathological entity.

Can chronic appendicitis be determined by a microscopic study of sections? An acute inflammation can be diagnosed by the presence of large numbers of pus cells throughout the tissue with varying numbers of other cells brought out later in the stage of repair, such as eosinophiles, round cells, plasma cells, and fibroblasts. A subacute inflammation is diagnosed in much the same way, but when we attempt to determine the earmarks of a chronic inflammation of the appendix we immediately encounter difficulties which appear to be insurmountable. The mucosa and lymphoid coats of the appendix undergo many changes during life which must be considered within normal limits.

In studying appendices microscopically, eosin-

CHART No II MACROSCOPIC — NATURE OF CASES		NUMBER	SIZE	CONTENTS					ADHESIONS ETC.					ATROPHIC OBLITERATIVE CHANGES	TOTAL GROSS PATHOLOGY	
				1	MUCUS-BLOOD OR PUS	THIN FECES	FECOLITHS	FOREIGN BODIES	1	+	++	KINKS	JACKSONS VEIL		PRESENT	ABSENT
1 APPENDICITIS CHRONIC	No	81	6x.9 cm	15	20	38	6	2	59	9	9	4	2	4	28	53.
	%	40		18.5	24.6	47	7.4	2.4	73	11.1	11.1	5	3	5	34	66
2 CHOLECYSTITIS	No	12	7.3x.6 cm	6	2	3	1	0	10	—	—	—	2	3	—	—
	%	5.9		50	16.6	25	8.3		83				16	25		
3 SALPINGITIS	No	14	5x.8 cm	3	4	7	0	0	8	3	3	1	—	3	—	—
	%	6.9		21.4	28.5	50			57	21.4	21.4	7		21		
4 UTERINE SURGERY	No	25	5.5x.6 cm	5	3	14	3	0	21	2	1	—	1	1	10	15
	%	12.3		20	12	56	12		84	8	4		4	4	40	60
5 HERNIA	No	7	6.3x.6 cm	2	2	2	1	0	7	—	—	—	—	1	—	—
	%	3.4		28.5	28.5	28.5	14.2		100					14		
6 MISCELLANEOUS	No	63	5.7x.7	20	17	17	7	2	56	4	2	1	—	3	26	37
	%	31.2		31.7	27	27	11	3.1	88.8	6.3	3	1.5		4.7	41	59

ophiles are found in large numbers, located chiefly in the mucosa. Occasionally there is found a few polynuclear leukocytes. My records reveal no noticeable difference in these findings in clinically diagnosed chronic appendicitis, and Groups 2-6 of my series. Leukocytes are never numerous in the mucosa and deeper tissues and only slightly more frequent in chronic appendicitis than in the control groups of apparently normal appendices.

A study microscopically of the thickness of the various histological layers of the appendiceal wall reveals no variation in the lymphoid and submucous coats and only a slight thinning of the muscular coat.

The microscopical findings in chronic appendicitis as diagnosed clinically fail to reveal anything pathologically specific, or that are not found in appendices without symptoms.

What changes are found in the obliterated and atrophic appendix? The number in this class is too small for definite conclusions. In this study, however, the percentage with these changes is higher in Groups 2-6 than in Group 1 with clinically chronic appendicitis. Of the fifteen patients of all the groups the history reveals a previous acute attack in at least twelve. With an 80 per cent positive history, and our knowledge of the degenerative changes occurring in the lining of this organ during an acute attack, it may be readily seen how the destroyed mucosa is replaced by adhesion of the raw surfaces and obliteration of the lumen. Apparently only a small percentage of these appendices cause further symptoms, and microscopically no evidence of inflammation remains other than obliteration of the lumen.

What is the rôle of eosinophiles in the normal and chronic appendicitis? Eosinophiles in the tissues are usually looked upon as a sign of chronic inflammation. They are found in the lymph nodes of Hodgkin's disease, in the cervix associated with inflammatory lesions and malignancy, and in the walls of pus tubes and infections of the gonorrheal type. They are also found in the secretions of bronchial asthma, in polypi, and inflammation of the mucous membranes of the nose and throat, as well as in many other conditions.

Eosinophiles were present in the mucosa of all my cases in Group 1, while in Groups 2-6 they are found in over 95 per cent. With further sections and study this percentage would be somewhat higher, as I have failed to find an appendix which possesses a mucosa in which varying numbers of eosinophiles cannot be demonstrated. The conclusion seems obvious, therefore, that eosinophiles in the appendiceal mucosa is a normal condition, or that over 95 per cent of people generally suffer from chronic appendicitis. On the other hand, if eosinophiles in the appendiceal mucosa does not always denote inflammation there must be some reason for their invariable presence. They may be associated with the protective mechanism or with the glands of internal

CHART NO. III
MICROSCOPIC

NATURE OF CASES		NUMBER	MUSCLE COAT			SUBMUCOSA			LYMPHOID				MUCOSA								
													EOSINOPHILES					POLYNUCLEARS			DEEP INFILTRATION OF EOSINOS & POLY'S
			NORMAL	THIN	+ +	NORMAL	THIN	+ +	NORMAL	THIN	+	+ +	1	FEW	+	+ +	+ + +	1	OCCASIONAL	+	
1 APPENDICITIS CHRONIC	No	81	18	25	23	28	10	43	27	9	23	12	0	8	17	31	17	14	6	61	23
	%	40	27	38	35	35	12	53	38	12.6	32.3	17		11	23	42	23	17	7.4	75	28.3
2 CHOLECYSTITIS	No	12	4	4	3	2	6	4	5	3	4	5	3	1	2	2	4	6	2	4	4
	%	5.9	36	36	27	17	50	33	41	25	34		25	8	16.5	16.5	33	50	16.5	33	33.5
3 SALPINGITIS	No	14	1	4	9	5	3	6	3	1	7	3	2	1	5	3	3	7	-	7	2
	%	6.9	7	28.5	64	36	21.5	42.5	21	7	49	21	14	7	35.5	21	21	50	0	50	14
4 UTERINE SURGERY	No	25	10	5	10	6	6	13	7	3	7	8	2	4	5	9	5	1	21	3	13
	%	12.3	40	20	40	24	24	52	28	12	28	32	8	16	20	36	20	4	84	12	52
5 HERNIA	No	7	1	3	3	4	1	2	2	2	3	-	1	0	2	2	2	4	1	2	1
	%	3.4	14	43	43	57	14	28.6	28.5	28.5	43		14		28	28	28	57	14	28	14
6 MISCELLANEOUS	No	63	15	19	29	13	12	38	26	7	18	12	3	2	19	23	16	15	6	42	15
	%	31.2	24	30	47.6	20.6	19	60.4	41	11	29	19	4.7	3	30	36.6	25.5	24	9	68	24

secretion. There is no evidence to indicate internal secretion from the appendix. This brings up the question of, "what is the function of the appendix?" Many theories have been advanced, most of them promptly disproved, but I believe that if this subject were better understood the question of the eosinophiles would be answered. If the appendix secretes mucus the problem is simpler, as eosinophiles are very closely associated with mucus formation, and are found chiefly in mucous membranes. I conclude, therefore, that the presence of eosinophiles in the mucous membrane of the appendix is normal.

A few items of general interest are brought out by this study. Of the 202 consecutive cases 80 per cent were females. The blood count in chronic appendicitis gave an average of 12,660 white cells, and the percentage of polynuclears is somewhat elevated, while in Groups 4, 5, and 6, the leukocyte count is quite normal. The average count for cholecystitis and salpingitis approached that of chronic appendicitis.

Although this study is incomplete, I believe the findings justify at least in part the following conclusions regarding pathological conditions in appendices removed by operation:

1. Chronic appendicitis often is a clinical condition resting more on a functional than a pathological basis.

2. Obliterative and atrophic appendices are the result of previous acute pathological processes and are not found in increased numbers in cases diagnosed clinically as "chronic appendicitis."

3. Eosinophiles in the mucosa of the appendix is no indication of chronic appendicitis, but is probably a link in the defensive mechanism and is normal.

4. Eosinophiles and leukocytes in the submucosa and muscularis is positive evidence of inflammatory changes in the appendix.

5. Chronic appendicitis cannot be determined in more than an extremely small percentage of instances by the histological examination alone.

6. Complete data on gross findings at operation are essential to a correct diagnosis.

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